

ABSTRACT

The present invention is directed to identification of agents that modulate UBP43 activity as well as associated methods, uses, processes, compositions and agents. In particular, the invention is directed to *in vivo* and *in vitro* methods to identify an agent that inhibits or stimulates UBP43 activity within a cell, a method for inducing cellular apoptosis, a method for affecting cellular reaction to interferon, a method for treating disease associated with cellular proliferation by causing apoptosis, and a method for treating both acute and chronic diseases in which interferon exerts a beneficial effect. The invention is also directed to modified ISG15-conjugates that have lowered or no susceptibility to UBP43 cleavage, pharmaceutical compositions of the agents, conjugates, and additional modified ISG15-conjugates.